UNITED STATES PATENT AND TRADEMARK OFFICE

clc

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/376,604	08/18/1999	RAGUPATHY MADIYALAKAN	AREX-P03-004	6693

7590 01/05/2006

Matthew P Vincent
Ropes & Gray
One International Place
Boston, MA 02110

EXAMINER	
NICKOL, GARY B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/376,604	MADIYALAKAN ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *243,244 and 247-250* is/are withdrawn from consideration.

5)☒ Claim(s) *276-278* is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *125,129,130,187,191,192,274 and 275* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 113,117-120,123,125,129-131,133-135,137-139,141-144,170-174,180-182,187,190-193,195,197-204,206-209,236,237,239,241-244,247-251 and 254-278.

Continuation of Disposition of Claims: Claims rejected are 113,118-120,131,133-135,137-139,141-144,170-174,180-182,190,193,195,197-204,206-209,236,237,239,241,242,251 and 254-273.

Re: Madiyalakan *et al.*

Date of priority: 06-17-1999

Response to Amendment

The Amendment filed 11-28-2005 in response to the Office Action of 07-29-2005 is acknowledged and has been entered.

New claims 274-278 were added.

Claims 113, 117-120, 123, 125, 129-131, 133-135, 137-139, 141-144, 170-174, 180-182, 187, 190-193, 195, 197-204, 206-209, 236-237, 239, 241-244, 247-251, 254-278 are pending.

Claims 243-244, 247-250 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 113, 117-120, 123, 125, 129-131, 133-135, 137-139, 141-144, 170-174, 180-182, 187, 190-193, 195, 197-204, 206-209, 236-237, 239, 241, 251, and 254-278 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejection Withdrawn:

The rejection of Claims 113, 117-120, 123, 131-135, 137-139, 141-144, 170-174, 180-182, 185, 190, 193-195, 197-204, 206-209, 235-239, 241-242, 251, 260-261, 264-265, 268-269, 272-273 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 5,532,159 (Webb *et al.* April 1, 1994) has been withdrawn. In an interview conducted 11-08-05, applicant's provided evidence and convincing reasoning that Webb *et al.* reference did not inherently teach the induction of an a host immune response. Furthermore, the declaration filed under 37 CFR 1.132 (filed 11-28-05) by Dr. Birgit C. Schultes attests to the latter. Specifically, the examples in Webb *et al.* do not teach the induction of a host T-cell response and or host humoral response upon administration of an anti-OFP antibody. Webb *et al.* discloses the administration of a single 100 ug to 165 ug dose of anti-OFP antibodies to 50 day old female rats bearings DMBA-induced tumors (columns 11-12). As shown in Table I, in all but three cases, the tumor volume decreased within one day after the injection of antibody. To those of skill in the art, these results show that the antibody either had a direct effect on the tumor or unleased an already existing but suppressed immune response. In contrast, it is well known in the art of immunology, that induction of an immune response requires at least 5-7 days to elicit an initial T cell response and or at least 5-20 days to elicit a humoral immune response. Thus, the reference as a whole indicates that these antibodies do not elicit an immune response against OFP.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

New Rejections:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 113, 118-120, 131, 133-135, 137-139, 141-144, 170-174, 180-182, 190, 193, 195, 197-204, 206-209, 236-237, 239, 241-242, 251, 254-261, 263-269, 271-273 rejected under 35 U.S.C. 102(b) as being anticipated by US 5,725,856 (Hudziak *et al.*, March 10, 1998) as further evidenced by Ward *et al.*, "Unconjugated antibodies for cancer therapy: lessons from the clinic", Cancer Treatment Reviews, 1997, Vol. 23, pages 305-319 and Leitzel *et al.* "Elevated Soluble c-erbB-2 Antigen Levels in the Serum and Effusions of a Proportion of Breast Cancer Patients, Jnl.Clin.Oncol., 1992, Vol. 10. No. 9, pages 1436-1443.

Hudziak *et al.* teaches methods of administering non-radiolabeled antibodies specific for the Her2/neu antigen (a self-protein receptor associated with human cancer), or more specifically, to the extracellular domain (ECD) of HER2/neu for the purposes of treating cancer. This includes parenteral and intravenous administration ranging from 0.1 to 10mg/kg (i.e., 100μg to 10,000μg per kg) of patient body weight. (column 7, lines 35-45).

As evidenced by Ward *et al.*, the Her2/neu antigen is "shed" from tumor cells (see page 311, Table 4). Furthermore, Leitzel *et al.* teach elevated levels of the extracellular domain of soluble her2/neu in the *sera* from cancer patients.

With regards to inducing an immune response via the administration of anti-Her2/neu antibodies, Ward *et al.* teach that the mechanism of action includes ADCC and CMCC reactions (page 309, Table 2, & top of page 307). Furthermore, Hudziak *et al.* teach (column 10, lines 35+) that upon complexing with growth factor receptors, the antibodies can induce serum complement and or ADCC. Also, Ward *et al.* teaches that anti-Her2 antibody administration includes contacting the antigen and the antibody at least two times (page 309, Table 2).

The specification of the present application teaches [para 125] that compositions of the present invention may initiate *direct* mechanisms for killing undesirable cells such as cancer cells via antibody-dependent cell-mediated cytotoxicity (ADCC) or indirectly, via complement-mediated cytotoxicity (CDC). Hence, the in-vivo administration of anti-HER2 antibodies for the purposes of treating cancer encompasses the activation of an effective host T cell response or a humoral immune response.

Hudziak *et al.* further teach that the composition comprises one or more adjuvants, one or more carriers, one or more excipients, one or more stabilizers, one or more pharmaceutically acceptable carriers and or physiologically acceptable saline (column 11, lines 45+). The reference further teaches murine or mouse antibodies, human antibodies, chimerics, and genetically engineered antibodies (column 10).

While the above references do not specifically teach that the immune complex formed between the antibody and antigen "results in the presentation of other epitopes on the antigen to the host's immune system", the method steps described in the prior art comprise the same steps as claimed in the instant invention and the claimed functional limitations would be an inherent property of the referenced method. Thus, it does not appear that the claim language or limitation

results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 262 and 270 are further rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,725,856 (Hudziak *et al.*, March 10, 1998).

Hudziak *et al.* teaches as set forth above.

Hudziak *et al.* does not specifically teach administration of the antibodies "at least two times".

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer the antibodies of Hudziak *et al.* at least two times (or more

than once) in order to effectively eliminate or reduce the patient's tumor burden. One would have been motivated to do so because determining the effective dose is well within the level of ordinary skill in the art. Furthermore, it is well within the level of ordinary skill in the art to determine optimum concentrations of reactants. See In re Kronig, 190 USPQ 425.

Claim Objections

Claims 125, 129-130, 187, 191, 192, and 274-275 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

Claims 276-278 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER